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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,893	12/01/2000	Dennis Bigg	427 038	9852

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EXAMINER

COLEMAN, BRENDA LIBBY

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 08/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/701,893

Applicant(s)

BIGG et al.

Examiner

Brenda Coleman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 5, 2003
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3, 4, and 9-13 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3, 4, and 9-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

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DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on March 18, 2003 and March 24, 2003 have been entered.

Claims 3, 4 and 9-13 are pending in the application.

This action is in response to applicants' amendments dated March 18, 2003 and March 24, 2003. Claims 9-11 have been amended.

Response to Arguments

Applicants' arguments filed March 18, 2003 and March 24, 2003 have been fully considered with the following effect:

1. The applicants' amendments and arguments are sufficient to overcome the 35 U.S.C. § 112, first paragraph rejection maintained in the office action dated August 8, 2002, which is hereby **withdrawn**.
2. The applicants' amendments and arguments are sufficient to overcome the 35 U.S.C. § 112, second paragraph rejection maintained in the office action dated August 8, 2002, which is hereby **withdrawn**.

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3. The applicant's amendments and arguments are sufficient to overcome the 35 USC § 102, anticipation rejections labeled 3, 5, 6 and 7 maintained in the office action dated August 8, 2002, which are hereby **withdrawn**. However, with regards to the 35 U.S.C. § 102, anticipation rejections labeled 4 and 8 of the last office action, the applicant's amendments and remarks have been fully considered but they are not persuasive.

4. The applicants' stated that "this is excluded by the ii) disclaimer of 4-hydroxy-phenyl in the definition of R'". However the compound taught by Girault is where R₁ is para-chloro which is not excluded by the proviso of claim 11.

Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Girault et al., Chromatographia. For reasons of record and stated above.

8. The applicants' stated that "the closest compounds are excluded by the disclaimer iiiii)". However the compounds taught by Okano is where W is 4-fluorophenyl-CH₂-C(O) and phenyl-CH₂-C(O) which is not excluded by the proviso of claim 11.

Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Okano et al., EP 0 367 110. For reasons of record and stated above.

4. The applicant's amendments and arguments are sufficient to overcome the 35 USC § 103, obviousness rejection maintained in the office action dated August 8, 2002, which is hereby **withdrawn**.

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5. The applicant's amendments and arguments are sufficient to overcome the 35 U.S.C. § 112, second paragraph rejections labeled a), b), c), d) and e) of the office action dated August 8, 2002, which are hereby **withdrawn**. However, with regards to the 35 U.S.C. § 112, second paragraph rejections labeled f) and g) the applicant's amendments and remarks have been fully considered but they are not persuasive.

- f) The applicants' stated that "claim 13 is now dependent on claim 11". However, the claim has not been amended. The applicants requested that the amendments filed March 18, 2003 and March 24, 2003 be entered with the filing of their RCE, however, the amendment correcting the claim dependency of claim 13 was filed January 13, 2003 and has not been entered.
- g) The applicants' stated that "the missing element Y' has been supplied therein". However, the claim has not been amended. The applicants requested that the amendments filed March 18, 2003 and March 24, 2003 be entered with the filing of their RCE, however, the amendment correcting the missing element Y' was filed January 13, 2003 and has not been entered.

Claim 13 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For reasons of record and stated above.

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In view of the amendment dated April 21, 2003, the following new grounds of rejection apply:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 9-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

- a) The definition of R₃ in claim 10 includes a moiety which is not described in the specification, i.e. heteroalkylalkyl. See line 16 on page 2 of the amendment filed March 18, 2003.
- b) The amendment to the proviso labeled iiiii) in claim 11 includes species when X is -CH₂- which are not described in the specification. See lines 21-23 on page 14 of the specification.

Applicant is required to cancel the new matter in the reply to this Office action.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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7. Claims 3, 4 and 9-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a) Claim 11 is vague and indefinite in that it is not known what is meant by the definition of the substituents on the R' group which includes -CN phenyl. It is believed that the applicants intended -CN, phenyl. See line 6 on page 2 of the amendment filed March 24, 2003.
- b) Claim 11 is vague and indefinite in that there is no definition for the variable R'₃. See line 2 on page 1 of the amendment filed March 24, 2003.
- c) Claim 11 is vague and indefinite in that it is not known what is meant by a W' in the first proviso. It is believed that the applicants intended a) W'. See line 10 on page 2 of the amendment filed March 24, 2003.
- d) Claim 11 is vague and indefinite in that it is not known what is meant by 0chlorine in the first proviso. See line 11 on page 2 of the amendment filed March 24, 2003.
- e) Claim 11 is vague and indefinite in that it is not known what is meant by 0-chloro in the definition of R'₁. See line 16 on page 2 of the amendment filed March 24, 2003.
- f) Claim 11 is vague and indefinite in that it is not known what is meant by R'₃ in the proviso labeled ii). It is believed that the applicants intended R'₃. See line 17 on page 2 of the amendment filed March 24, 2003.

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- g) Claim 11 is vague and indefinite in that it is not known what is meant by Y in the proviso labeled iii). There is no variable Y in formula II. It is believed that the applicants intended Y'. See line 20 on page 2 of the amendment filed March 24, 2003.
- h) Claim 11 is vague and indefinite in that it is not known what is meant by 0-chlorine in the definition of R'₁. See line 20 on page 2 of the amendment filed March 24, 2003.
- i) Claim 11 is vague and indefinite in that it is not known what is meant by the definition of X' in the proviso labeled iiiii). X' is divalent, however, the moiety CH₂CH₂ is missing one of it's points of attachment. See line 23 on page 2 of the amendment filed March 24, 2003.
- j) Claim 11 is vague and indefinite in that it is not known what is meant by Y in the proviso labeled iiiiii). There is no variable Y in formula II. It is believed that the applicants intended Y'. See line 22 on page 2 of the amendment filed March 24, 2003.
- k) Claim 11 is vague and indefinite in that it is not known what is meant by the proviso labeled iiiiii). It is included in the proviso labeled iiiiii). See lines 1-2 on page 3 of the amendment filed March 24, 2003.
- l) Claim 11 is vague and indefinite in that it is not known what is meant by the variables R_{2a}' and R_{2b}' in the proviso labeled iiiiii). It is believed that the

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applicants intended R_{2a} and R_{2b} . See line 3 on page 3 of the amendment filed March 24, 2003.

- m) Claim 9 recites the limitation "a composition" in the preamble of the claim. There is insufficient antecedent basis for this limitation in the claim. Claim 9 is a composition claim which is dependent on a method of use claim.
- n) Claim 10 is vague and indefinite in that it is not known what is meant by the variable W in formula I which is not defined within the claim. See line 1 on page 2 of the amendment filed March 18, 2003.
- o) Claim 10 is vague and indefinite in that it is not known what is meant by the definition of W_1 . There is no variable W_1 in formula I. See line 2 on page 2 of the amendment filed March 18, 2003.
- p) Claim 10 is vague and indefinite in that it is not known what is meant by the definition of the substituents of R which includes a divalent moiety, i.e. $-CF_3-$. See line 4 on page 2 of the amendment filed March 18, 2003.
- q) Claim 10 is vague and indefinite in that it is not known what is meant by the definition of R_{2a} and R_{2b} which are individually hydrogen or methyl R_3 . It is believed that the applicants intended to insert a comma after methyl. See line 10 on page 2 of the amendment filed March 18, 2003.

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- r) Claim 10 is vague and indefinite in that it is not known what is meant by the definition of R_3 which includes the moiety aryloxalkyl. See line 15 on page 2 of the amendment filed March 18, 2003.
- s) Claim 10 is vague and indefinite in that it is not known what is meant by the variables R_{22} and R_{23} which are not defined within the claim. See line 1 on page 3 of the amendment filed March 18, 2003.
- t) Claim 10 is vague and indefinite in that it is not known what is meant by the moiety S- in the definition of Z_{31} which a divalent variable, however, the moiety S- is not. See line 2 on page 3 of the amendment filed March 18, 2003.
- u) Claim 10 is vague and indefinite in that it is not known what is meant by the definition of R_{32} and R_{33} . There are no variables R_{32} and R_{33} in formula I. See line 3 on page 3 of the amendment filed March 18, 2003.
- v) Claim 10 is vague and indefinite in that it is not known what is meant by the first word in line 4, i.e. selected. See line 4 on page 3 of the amendment filed March 18, 2003.
- w) Claim 10 is vague and indefinite in that it is not known what is meant by the moiety heterocycloalkyl in the definition of R_{32} and R_{33} . See line 5 on page 3 of the amendment filed March 18, 2003.
- x) Claim 10 recites the limitation "said conditions" in the last line of the claim. There is insufficient antecedent basis for this limitation in the claim.

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- y) Claim 12 recites the limitation "hydrogen or R-X-C(Y)-" in the definition of W, however, there is no definition of W in claim 10. There is insufficient antecedent basis for this limitation in the claim.
- z) Claim 12 recites the limitation "lower alkyl" in the definition of R_{2a} and R_{2b}. There is insufficient antecedent basis for this limitation in the claim. See line 1 on page 2 of the amendment filed May 31, 2002.
- aa) Claim 12 recites the limitation "heteroarylalkyl" in the definition of R₃. There is insufficient antecedent basis for this limitation in the claim. See line 4 on page 2 of the amendment filed May 31, 2002.
- ab) Claim 12 recites the limitation "cycloalkyl" in the definition of R₃. There is insufficient antecedent basis for this limitation in the claim. See line 4 on page 2 of the amendment filed May 31, 2002.
- ac) Claim 12 recites the limitation "heteroaryl" in the definition of R₃. There is insufficient antecedent basis for this limitation in the claim. See line 4 on page 2 of the amendment filed May 31, 2002.
- ad) Claim 12 recites the limitation "NR₃₂R₃₃" in the definition of R₃. There is insufficient antecedent basis for this limitation in the claim. See line 6 on page 2 of the amendment filed May 31, 2002.
- ae) Claim 3 recites the limitation "hydrogen or R-X-C(Y)-" in the definition of W, however, there is no definition of W in claim 10. There is insufficient antecedent

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basis for this limitation in the claim. See line 2 of claim 3 in the amendment filed May 31, 2002.

- af) Claim 3 recites the limitation "indolylmethyl" in the definition of R_3 . There is insufficient antecedent basis for this limitation in the claim. See line 16 on page 7 of the amendment filed May 31, 2002.
- ag) Claim 13 recites the limitation "W" in formula II. There is insufficient antecedent basis for this limitation in the claim. See line 12 on page 11 of the amendment filed May 31, 2002.
- ah) Claim 4 recites the limitation "3-indolyl-methyl" in the third species on page 45. There is insufficient antecedent basis for this limitation in the claim. See lines 5-6 on page 45 of the specification.
- ai) Claim 4 is vague and indefinite in that it is not known what is meant by 2-terBu in line 12 on page 47 of the specification.
- aj) Claim 4 recites the limitation "3-indolyl-methyl" in line 18 on page 48 of the specification. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Okano et al., EP 0 367 110. The generic structure of Okano encompasses the instantly claimed compounds, see the Formula on page 3. Examples 89 and 97 which anticipate some of the compounds of the instant invention differ only in the nature of the Y and X substituents. Page 3, line 42 defines the substituent X as a group of the formula -O-C(O)-, a group of the formula -N(R⁵)-C(O)-, a group of the formula -C(O)-, a group of the formula -O-P(O)(OR⁶)- and a group of the formula -SO₂- and Y is a cycloalkyl group, a cycloalkylalkyl, an alkynyl group, a group of the formula CH₃-C(CN)(R⁷)-(CH₂)_p, a group of the formula NC-(CH₂)_p-, arylalkyl, etc. Compounds of the instant invention are generically embraced by Okano in view of the interchange ability of Y and X substituents of the tetracyclic ring system. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example Y is pyridyl as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

9. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Braquet et al., FR 2 660 311. The generic structure of Braquet encompasses the instantly claimed compounds, see Formula I on page 1. The examples 6-23, 29, etc. differ only in the nature of the Y and R substituents. Page 1, line 9 defines the substituent Y and an oxygen or sulfur atom and R as a lower straight alkenyl group up to C₅, a straight or branched alkyl group up to C₂₀ or cyclic up to

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C₆, an aryl or heteroaryl substituted straight or branched alkyl group up to C₅, a phenyl group substituted by one or several alkyl groups, or lower alkoxy groups up to C₅, a phenoxy group, a lower alkyl sulfonyl group up to C₅, or fluorine or chlorine atoms, or trifluoromethyl groups, etc. Compounds of the instant invention are generically embraced by Braquet in view of the interchange ability of Y and R substituents of the tetracyclic ring system. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example R is pyridyl as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

10. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Weber et al., EP 0 503 471. The generic structure of Weber encompasses the instantly claimed compounds, see Formula Ia on page 18. The examples of Table spanning pages 19-28 differ only in the nature of the R², R³, R⁴ and R⁵ substituents. The substituents R² and R³ are hydrogen or methyl, R⁴ is a phenyl ring mono- or polysubstituted by methyl, halogen, nitro, alkoxy and/or trifluoromethyl and R⁵ is an optionally substituted C₁₋₈alkyl, an optionally substituted aryl group, CH₂-aryl or CH₂-CH₂-aryl group. Compounds of the instant invention are generically embraced by Weber in view of the interchange ability of the R², R³, R⁴ and R⁵ substituents of the tetracyclic ring system. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example R⁵ is 4-nitrophenyl as well as other possibilities from the

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generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is (703) 305-1880. The examiner can normally be reached on Mondays from 8:30 AM to 5:00 PM, on Tuesdays from 8:00 AM to 4:30 PM, on Wednesday thru Friday from 9:00 AM to 5:30 PM.

The fax phone number for this Group is (703) 308-4734 for "unofficial" purposes and the actual number for **OFFICIAL** business is **308-4556**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.



Brenda Coleman
Primary Examiner AU 1624
August 1, 2003